REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 10-12 and 14-18 will be pending in the application subsequent to entry of this Amendment.

Two important matters have not been addressed in the Office Action Summary of the present Official Action or the Office Action Summary of the previous Official Action dated June 4, 2007.

Application Papers/Drawings

This application as filed contains two sheets of drawings however the Office has not indicated that the drawings have been accepted. As they originated from the PCT and were approved by the PCT and this is a national stage filing, counsel assumes that the drawings are acceptable. The examiner is requested to confirm acceptability of the drawings in the next communication.

Claim for Benefit of Priority/Certified Copy

Both the current Official Action and the previous Official Action of June 4, 2007 in the Office Action Summary did not acknowledge receipt of a certified copy of the underlying Italian priority application. According to the communication dated March 15, 2006, the U.S. as a receiving office did receive a copy of the priority documents on May 18, 2005; *see* "Notice of Acceptance of Application ..." mailed March 15, 2006.

As the Office has already acknowledged receipt of the priority document the examiner is requested in the next communication to indicate that all of the priority documents including certified copies have been received.

Claim Amendments

Claim 10 is amended to identify specific conditions in a grouping that finds basis in the description of the invention in the paragraph bridging pages 3 and 4 of the specification. This serves to make the claims more precise, claim 1 being the only independent claim, and to advance examination of this application. No new subject matter is presented. As a consequence of this change, claim 13 has been deleted the subject matter of which is now incorporated in claim 10.

Response to Prior Art-Based Rejection

To establish a case of *prima facie* obviousness, all of the claim limitations must be taught or suggested by the prior art. *See* M.P.E.P. § 2143.03. A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing the legal standard provided in *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. *See id.* ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. *See id.* at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a *prima facie* case of obviousness under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn*, 78 USPQ2d at 1335; *see KSR*, 82 USPQ2d at 1396. A claim which is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* at 1396. Finally, a determination of *prima facie* obviousness requires a reasonable expectation of success. *See In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

All pending claims were rejected under Section 103(a) as allegedly unpatentable over Cavazza '812, Cavazza '378 and DeFelice in view of DeSimone and Xiu, all U.S. patents.[1] Applicants traverse.

The combination of all five of these patents do not render obvious the claimed invention because all limitations of independent claim 10 are not fairly taught or suggested in the cited patents. Moreover, claims depending from this independent claim are also not made obvious by the documents because the limitations of an independent claim are incorporated in their dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Cavazza US 4,474,812 refers to the use of L-carnitine (LC) for improving of the biochemical and behavioral parameters which are regarded as peculiar to senility (col.1, lines 6-10). Cavazza '812 does not disclose the combination of propionyl LC with acetyl LC.

Cavazza US 6,245,378 refers to the combination of LC, acetyl LC and propionyl LC for facilitating the adaption of skeletal muscle to strenuous exercise (abstract). Considering each of the five citations individually, Cavazza '378 does not disclose the list of disorders of newly amended claim 10.

De Felice US 3,830,931 discloses the use of carnitine for treating old patients with heart failure. De Felice does not teach the combination of propionyl LC with acetyl LC.

De Simone US 6,037,373 discloses the use of at least one acyl carnitine being acetyl LC, isovaleryl LC, propionyl LC for increasing IGF-1 levels and treating cytological diseases including: neuropathies of the optic nerve and of the olfactory nerve, neuralgia of the trigeminal nerve, Bell's paralysis, amyotrophic lateral sclerosis and other motor neuron diseases,

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[1] It is noted that five references have been asserted as the basis of the Examiner's obviousness rejection. As the courts have stated, the fact that it is necessary to cite such a large number of references is, in and of itself, indicative of non-obviousness. *Minneapolis-Honeywell Regulator Company v. Midwestern Instruments, Inc.*, 298 F.2d 36, 38, 131 U.S.P.Q. 402, 403 (7th Cir. 1961); *The Ric-Wil Company v. E.B. Kaiser Company*, 179 F.2d 401, 404, 84 U.S.P.Q. 121, 124 (7th Cir. 1950); *Reynolds et al v. Whitin Machine Works*, 167 F.2d 78, 83, 76 U.S.P.Q. 551, 555 (4th Cir. 1948); and *Racal-Vadic, Inc. v. Universal Data Systems*, 1980 U.S. Dist. LEXIS 15864, *81, 207 U.S.P.Q. 902, 927 (N.D. Ala. 1980). Indeed, the inference that can be taken from the large reference citation is that not one reference is on point and that the patentee has clearly accomplished what the prior art has repeatedly failed to do. *Minneapolis-Honeywell Regulator Company v. Midwestern Instruments, Inc.*, 298 F.2d 36, 38, 131 U.S.P.Q. 402, 403 (7th Cir. 1961).

degeneration of the retina, osteoporosis, arthropathy, arthritis, cervical spondylosis and hernia of the intervertebral discs, clinical syndromes of reduced height, cachexia, acute or chronic hepatic necrosis, Turner's syndrome, sarcopoenia, growth hormone insensitivity syndromes, diabetes, obesity, asthenia in general and in particular myasthenia and heart asthenia, immunodeficiences and reperfusion injuries, cicatrization of wounds, healing of ulcers, the treatment of burns, tissue regeneration in general and in particular that of cutaneous, intestinal and hepatic tissue, and the formation of dentine (col. 1, lines 40-54).

De Simone does not mention the diseases of newly amended claim 10.

Xiu US 6,399,116 disclose that the *Rhodiola crenulata* can be in combination with anti-oxidants as carnitine (col. 3, line 19). Xiu discloses that *Rhodiola crenulata*, a variety of useful and beneficial effects, including: enhancing blood oxygen and nutrients levels, through enhancing oxygen transport, to enhance working capacity and endurance, to reduce muscle fatigue, to enhance memory and concentration, to reduce stress, to enhance cardiac and cardiovascular function, to provide antioxidant effects, to protect against oxidation, to provide anti-cancer effects, to promote DNA repair, to provide anti-radiation effects, to protect against radiation, to reduce inflammation, to increase insulin, to decrease levels of glucagon, to reduce histamine release, to reduce allergic reactions, preferably, to modulate testosterone levels, and to modulate sleep, especially to promote sleep, to modulate blood lipids, preferably, e.g., to lower cholesterol levels, to promote weight loss, and to enhance sexuability, such as improve sexual performance (col. 1, lines 8-25).

Xiu teaches that *Rhodiola crenulata* is the active agent which influence sexuability, while carnitine is an anti-oxidant.

Xiu does not refer to the combination of propionyl LC with acetyl LC.

The object of the present application is a method for treating the specified disorders caused by andropause by administering the combination of propionyl LC with acetyl LC.

The disorders caused by andropause include reduced libido or sexual drive and erectile function, also during the night, depression of mood, and lowering of intellectual activity, and spatial orientation capacity, as well as fatigue, irritability, reduced lean body mass, muscular capacity, mental concentration, and functioning of the hair-growing apparatus, increased visceral fat, atrophy of the skin, and reduced bone density resulting in osteopenia and

osteoporosis.

Andropause is caused by the progressive decrease in androgen production and is usually treated with estrogen replacement (page 1). Hormone treatment such as estrogen is full of drawbacks and adverse effect (page 2).

The results shown in the examples 1-20 of the present application, demonstrate that the treatment of patients with andropause by administering the claimed combination is as effective as estrogen replacement with testosterone undecanoate.

This means that the combination of propionyl LC with acetyl LC can be efficiently used to counteract the progressive lowering of androgen hormones, without incurring in the desired drawbacks and adverse effects typical of the oestrogen replacement therapy. These findings are not predictable form the prior art.

Only Cavazza '378 discloses the combination of acetyl LC and propionyl LC.

None of the cited documents refer to andropause i.e. the syndrome named "androgen decline in the aging male" (ADAM) or "partial androgen deficiency of the aging male" (PADAM) or "andropause" (The Aging Male, 4: 151-162, 2001), as defined in page 1 of the specification of this application.

This syndrome is related to aging but it is specifically due to an organic process and for this reason cannot be confused with oldness.

The claimed combination shows the essential features of acting as estrogen in raising androgen hormones levels, without drawbacks. This feature cannot be derived by the teachings of the prior art.

Presentation of Evidence

Attached is an evidentiary declaration, submitted under Rule 132 and signed by Mr. Aleandro Koverech as inventor, reporting new experimental data and support the present application.

In view of the above claims 10-12 and 14-18 are inventive over the cited prior art documents.

Withdrawal of the Section 103 rejection is requested because the claimed invention would not have been obvious to the ordinarily skilled artisan at the time Applicants made their invention.

Having responded to all of the pending rejections contained in the Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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